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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	44

Application Number	08/644,289
Filing Date	05/10/1996
First Named Inventor	Molly Kulesz-Martin
Art Unit	1642
Examiner Name	M. Davis
Attorney Docket Number	RPP:135D US

ENCLOSURES (*Check all that apply*)

- [x] Fee Transmittal Form
  - [x] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance Communication to a Technology Center (TC)
- [ ] Appeal Communication to Board of Appeals and Interferences
- [x] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual	Dunn & Associates
Signature	Michael L. Dunn
Date	Aug 11, 2003

CERTIFICATE OF TRANSMISSION/MAILING

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Typed or printed	Michael L. Dunn		
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PTO/SB/17 (01-03)
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FEE TRANSMITTAL for FY 2003

Effective 01/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 320.00

Complete if Known	
Application Number	08/644,289
Filing Date	05/10/1996
First Named Inventor	Molly Kulesz-Martin
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METHOD OF PAYMENT *(check all that apply)*

☑ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☐ Deposit Account:

Deposit Account Number: 04-1790

Deposit Account Name:

The Commissioner is authorized to: *(check all that apply)*

☐ Charge fee(s) indicated below ☐ Credit any overpayments

☑ Charge any additional fee(s) ~~during the pendency of this application~~

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =		X =
Independent Claims		- 3** =		X =
Multiple Dependent				=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	320.00
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,300	2453	650	Petition to revive - unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 320.00

SUBMITTED BY

(Complete *(if applicable)*)

Name (Print/Type)	Michael L. Dunn	Registration No. (Attorney/Agent)	25,330	Telephone	716-433-1661
Signature				Date	8-11-03

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This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, Washington, DC 20231.**

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RPP:135D US

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Molly F. Kulesz-Martin	Art Unit:	1642
Serial No:	08/644,289	Confirmation No:	4031
Filed:	May 10, 1996		
Examiner:	M. Davis		
For:	p53as PROTEIN AND ANTIBODY THEREFOR		

I certify that this **APPEAL BRIEF** is being deposited on **August 11, 2003** with the U.S.Postal Service as first class mail addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231

Michael L. Dunn
Registration No. 25,330

35
100
9/17/03

APPEAL BRIEF
(37 CFR 1.192)

Box AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants respectfully appeal the decision of the Examiner finally rejecting Claims 1, 3-6, 8-11, and 15-19 as set forth in the Office Action dated June 2, 2003. A Notice of Appeal was timely filed by the Applicants on July 17, 2003.

Real Parties in Interest

The real party in interest is Health Research, Inc. Assignee of the above application by assignment recorded in the Patent and Trademark Office at Reel 8019 Frame 0490.

Related Appeals and Interferences

An appeal has been filed on related patent application serial number 08/811,361 filed March 4, 1997.

Status of Claims

The application originally contained 15 claims. Claims 2 and 7 have been cancelled and Claims 12-14 have been withdrawn by the Examiner as being drawn to a non-elected invention. Claims 16-19 have been added by amendment. Claims 1 and 5 have been five times amended. Claims 15 and 16 have been twice amended. Claim 19 has been once amended. Claims 1, 3-6, 8-11, and 15-19 have been previously appealed and remanded to the Examiner by the Board of Patent Appeals and interferences. Claims 1, 3-6, 8-11, and 15-19 are again before the Board of Patent Appeals and interferences in the present appeal.

Status of Amendments

Claims 1, 5, 15, 16 and 19 have been amended. No amendments have been offered which have not been entered.

Summary of the Invention

A viral vector and a plasmid containing a cDNA sequence which encodes a protein designated p53as, said p53as being sequentially the same as wild type p53 up to the final 50 carboxy terminal amino acids of p53, said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to lack a negative regulatory domain of p53 for p53 specific DNA binding found within the last 50 amino acids at the p53 carboxy terminus, which negative regulatory domain must be activated in p53 for p53 to have active DNA binding, said

p53as and activated p53 binding to the same p53 DNA binding sequence AGGCATGCCT/AGGCATGCCT, SEQ. I.D. NO. 5, and said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to provide an epitope within said p53as which gives rise to an antibody which is reactive with the p53as but not with p53.

Issues Presented for Review

1. Whether claims 15-16 and 19 are patentable under 35 USC 112 first paragraph on the ground that the specification does not contain a written description sufficient to conclude that the Applicant had possession of the claimed invention at the time of filing.;

2. Whether claims 1, 3-4, and 17 are patentable under 35 U.S.C. 103 as being obvious over Han et al. (Nuc.AcidsRes. 20:1979-1981) in view of U.S. Patent to Sambrook et al.(Molecular Cloning, A Laboratory Manual, 2nd ed, Cold Spring Harbor Laboratory Press, pages 1.3, 1.21, Hupp et al. (Cell 71, 875-886) and Funk, WD et al.(Mol Cell Biol, 12:2866-2871); and

3. Whether claims 5-6, 8-11 and 18 are patentable under 35 U.S.C. 103 as being obvious over Han et al. (Nuc.AcidsRes. 20:1979-1981) in view of Lee et al (EP Patent Application 0-529-160).

Grouping of Claims

The claims do not stand or fall together. In the absence of the disclosure of the specification, the plasmid vector of claim 1 does not anticipate or suggest the viral vector of claim 5 or vice-versa. Further, the subclaims further restrict the independent claims to particular species, which species are not obvious over the independent claims in the absence of the disclosure of the specification. Further, in the absence of the disclosure of the specification, the

specific gene sequence of claim 15 is not suggested by claims 1 or 5. Furthermore, the specific embodiments in the subclaims are specifically not described in the cited art. Additionally, all claims are not subject to the same rejections.

Argument

The Examiner has rejected claims 15, 16 and 19 under 35 U.S.C. 112, first paragraph on the ground that the specification does not contain a written description sufficient to conclude that the Applicant had possession of the claimed invention at the time of filing.

The rejection of Claims 15-16 seems based upon the Examiner's argument that the claims are drawn to a plasmid containing a p53as gene sequence encoding the peptide of SEQ ID No. 1 or a portion thereof. The rejection of Claim 19 seems based upon the Examiner's argument that the claims are drawn to a viral vector containing a p53as gene sequence encoding the peptide of SEQ ID No. 1 or a portion thereof, which peptide will raise an antibody response. The Examiner has taken the position that this means that a peptide of essentially any length down to a few peptides is encompassed without sufficient description.

It is the Applicants' position that more than enough description is provided since the possible sequences are specifically taught and one skilled in the art can easily determine whether the particular sequence raises an antibody response without undue experimentation. There are only 18 amino acids in the peptide in question. It is a relatively simple matter to truncate the peptide from either or both ends and test the truncated peptide to determine whether it raises an antibody response. With only 18 starting amino acids, there would seem to be no more than about ten possibilities for a "portion" that will raise an antibody response. It is generally

believed that a peptide sequence must be at least 8 or 9 amino acids long before an antibody response is possible. In the case that an eight amino acid sequence could raise such a response, which is unlikely, there are only 55 possible sequences within SEQ ID No.1. There are only 36 possibilities in the case of sequences of ten or more. The disclosure of the base sequence (ID No. 1) with the statement that portions of the sequence that raise an antibody response are also included) is more than sufficient to support the genus.

The Examiner says "It is noted that claim 15 does not recite that the peptide would give rise to an antibody which is reactive with the p53as but not with p53, and thus the argument (with respect to raising an antibody) does not apply to claim 15."(material in parenthesis added) The Examiner again appears confused as to the law. The claim is intended to define the metes and bounds of the invention and the listing of the sequence of the specific novel peptide does just that and does it clearly. There is no requirement, as the Examiner seems to imply, that utility be set forth in the claims. Disclosure of utility is the province of the specification and the unobvious utility for the sequence is clearly stated in the specification. It is irrelevant the gene sequence may be long. In reality, DNA sequences, as found in chromosomes, are millions of base pairs long and many stated sequences are often part of a longer genomic sequence. It is sufficient that a unique peptide sequence is stated in the claim and clear utility for it is described in the specification.

The inventors should not be required to restrict their invention to exclude reasonable modifications that are well within the purview of the skilled artisan. These claims are not indefinite.

The rejection should be reversed.

Claims 1, 3-4, and 17 have been rejected by the Examiner as being obvious over Han et al. in view of Sambrook et al., Hupp et al. and Funk et al. This rejection should be withdrawn. As has been pointed out to the Examiner during prosecution, This rejection is a classic hindsight rejection where elements of the invention taught in the application are segregated, an attempt is made to find a reference each segregated element, the references are combined in hindsight to reconstruct the invention, and finally justification is sought for their combination after the combination is already made. In using this hindsight method, the Examiner has found it necessary to look for four different references to support at least four different hindsight segregated elements.

The Examiner has recognized that Han et al does not teach incorporation of a full p53as sequence into a plasmid , virus or any other vector and comes to the conclusion that there is a suggestion to look for such incorporation merely from the statement in Han et al. that "more precise biochemical and biological characterization of AS-p53 protein along with R-p53 protein appear to be critical in future studies of p53 function in normal cells and oncogenesis." It must be kept in mind that there are literally thousands of ways one might proceed with "more precise biochemical and biological characterization." Since Han et al did not actually form any proteins at all, formation of proteins based upon the disclosure of Han et al with respect to p53as was speculative. Whether or not the sequence contained inhibitors that prevented transcription or translation was not known, disclosed or suggested by Han et al. Zeroing in on incorporation of a complete p53as cDNA sequence into a plasmid as a way to proceed with "biochemical and

biological characterization" without any other such suggestion in Han et al. is classic impermissible hindsight.

Sambrook et al. generally discusses production and characterization of proteins but makes no suggestion as to any specific proteins and certainly not p53as protein. If one were to follow the logic of the Examiner, all future plasmids containing novel DNA sequences would be unpatentable because of the disclosure of generic procedures of Sambrook et al. and there need be no other reason for incorporating the sequence other than characterization of resulting protein, if in fact any is produced as a result of such incorporation. There needs to be some suggestion or reason in the art for incorporating a particular sequence into a plasmid or other vector to even want to do characterization of any protein that might result. **Neither Han et al., nor Sambrook et al. give any suggestion why one would want to incorporate a complete p53as into a plasmid from among myiads of other ways that one might proceed with characterization of p53as.**

In the last rejection the Examiner repeatedly states "The motivation is obvious." For reasons given above we do not agree that the "motivation is obvious", but even giving the Examiner the doubt, in making rejections under 35 U.S.C. 103, it is not sufficient that "motivation be obvious". For such a rejection to be proper, the result must be obvious. In the present case the result would not be obvious. One would not even have known whether the p53as alternatively spliced cDNA could be transcribed and then translated to form protein until it was tried. **Obvious to try (even if it were present) would not be obviousness.**

Hupp et al. similarly does nothing to cure the critical defects of Han et al.. There is nothing at all suggested in Hupp et al. that would make it obvious to incorporate a p53as cDNA into a plasmid. Hupp et al. appears not to be concerned with plasmids or any other vector.

The mere teaching of a DNA binding site by Funk similarly does not cure the critical defects described above.

This rejection is based upon an improper combination of references and even if the combination were proper, it would not disclose or suggest any embodiment of the presently claimed invention. The rejection should be reversed.

Claims 5-6, 8-11, and 18 have been rejected under 35 U.S.C. 103 as being obvious over Han et al. in view of Lee et al. This rejection is improper and should be withdrawn

This rejection is again a classic hindsight rejection where elements of the invention taught in the application are segregated, an attempt is made to find a reference each segregated element, the references are combined in hindsight to reconstruct the invention, and finally justification is sought for their combination after the combination is already made.

The Examiner has recognized that Han et al does not teach incorporation of a full p53as sequence into a plasmid , virus or any other vector and comes to the conclusion that there is a suggestion to look for such incorporation merely from the statement in Han et al. that "more precise biochemical and biological characterization of AS-p53 protein along with R-p53 protein appear to be critical in future studies of p53 function in normal cells and oncogenesis." It must be kept in mind that they are literally thousands of ways one might proceed with "more precise biochemical and biological characterization." Since Han et al did not actually form any proteins

at all, formation of proteins based upon the disclosure of Han et al with respect to p53as was speculative. Whether or not the sequence contained inhibitors that prevented transcription or translation was not known, disclosed or suggested by Han et al. Han et al. contains no disclosure or suggestion for incorporation of a full p53as sequence into a plasmid, let alone into a virus. Viruses are discussed for no purpose in Han et al. Zeroing in on incorporation of a complete p53as cDNA sequence into a virus as a way to proceed with "biochemical and biological characterization" without any other such suggestion in Han et al. is classic impermissible hindsight.

The extension to incorporation of a full p53as sequence into a virus by combination with Lee et al. is even farther afield. Lee et al suggests nothing at all concerning p53as and is directed to incorporation of entirely different sequences into viruses for purposes unrelated to the function of p53as. Lee et al. clearly does not cure the critical defect of Han et al.

If one were to follow the logic of the Examiner, all future viruses containing novel DNA sequences would be unpatentable because of the disclosure of generic procedures of Lee et al. and there need be no other reason for incorporating the sequence other than that entirely different sequences have been incorporated into viruses by Lee et al. There needs to be some suggestion or reason for incorporating a particular sequence into a virus or other vector to even want to do characterization of any protein that might result. **Neither Han et al., nor Lee et al. give any suggestion why one would want to incorporate a complete p53as into a virus from among myiads of other ways that one might proceed with characterization of p53as.**

In the last rejection the Examiner repeatedly states "The motivation is obvious." For reasons given above we do not agree that the "motivation is obvious", but even giving the Examiner the doubt, in making rejections under 35 U.S.C. 103, it is not sufficient that "motivation be obvious". For such a rejection to be proper, the result must be obvious. In the present case the result would not be obvious. One would not even have known whether the p53as alternatively spliced cDNA could be transcribed and then translated to form protein until it was tried. **Obvious to try (even if it were present) would not be obviousness.**

The purposes of Han et al. and Lee et al. are clearly different and have different functions and there is no reason to combine them except on the basis of hindsight and even then the presently claimed invention is not suggested. The rejection should be reversed.

Conclusion

In view of the foregoing, it is clear that the pending claims are patentable under 35 U.S.C. 112 and over the cited prior art. Reversal of the Examiner and allowance of all claims are therefore respectfully requested.

Respectfully submitted,

Dated: August 11, 2003

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MLD/cah
cc: P. Reczek
J. Jurkowski

Appendix

Reprinted below are the claims on appeal:

1. (previously presented) A plasmid containing a cDNA sequence which encodes a protein designated p53as, said p53as being sequentially the same as wildtype p53 up to the final 50 carboxy terminal amino acids of p53, said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to lack a negative regulatory domain of p53 for p53 sequence specific DNA binding found within the last 50 amino acids at the p53 carboxy terminus, which negative regulatory domain must be activated in p53 for p53 to have active DNA binding, said p53as and activated p53 binding to the same p53 DNA binding sequence AGGCATGCCT/AGGCATGCCT , SEQ. I.D. NO. 5 and said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to provide an epitope within said p53as which gives rise to an antibody which is reactive with the p53as but not with p53.

2. (canceled)

3. (original) The plasmid of Claim 1 wherein the p53as naturally occurs in a mammal.

4. (original) The plasmid of Claim 1 wherein the p53as is mouse p53as.

5. (previously presented) A viral vector containing a cDNA sequence which encodes a protein designated p53as, said p53as being wildtype p53 up to the final 50 carboxy terminal amino acids of p53, said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to lack a negative regulatory domain of p53 for p53 sequence specific DNA binding found within the last 50 amino acids at the p53 carboxy terminus, which negative regulatory domain must be activated in p53 for p53 to have active DNA binding, said p53as and activated p53 binding to the same p53 DNA binding sequence AGGCATGCCT/AGGCATGCCT, SEQ. I.D. NO. 5, and said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to provide an epitope within said p53as which gives rise to an antibody which is reactive with the p53as but not with p53.

6. (original) The viral vector of Claim 5 wherein the vector is baculovirus vector.

7. (canceled)

8. (original) The viral vector of Claim 5 wherein the p53as naturally occurs in a mammal.

9. (original) The viral vector of claim 6 wherein the p53as naturally occurs in a mammal.

10. (original) The viral vector of Claim 5 wherein the p53as is mouse p53as.

11. (original) The viral vector of Claim 6 wherein the p53as is mouse p53as.

12. (withdrawn) An antibody wherein the antibody is directed against at least a portion of human p53 intron 10 sequence encoding SLRPFKALVREKGHRPSHSC (SEQ. I.D. NO. 1).

13. (withdrawn) The antibody of Claim 12 wherein the antibody is a polyclonal antibody.

14. (withdrawn) The antibody of Claim 12 wherein the antibody is a monoclonal antibody.

15. (previously presented) A plasmid containing a p53as gene sequence encoding the peptide SLRPFKALVREKGHRPSHSC SEQ. ID.D NO. 1.

16. (previously presented) The plasmid of Claim 1 containing a p53as gene sequence encoding a portion of the peptide SLRPFKALVREKGHRPSHSC, SEQ. I.D. NO. 1, which peptide will raise an antibody response which gives rise to an antibody which is reactive with the p53as but not with p53.

17. (previously presented) A cell transfected with the plasmid of Claim 1.

18. (previously presented) A cell transfected with the viral vector of Claim 5.

19. (previously presented) The viral vector of Claim 5 containing a p53as gene sequence encoding a portion of the peptide SLRPFKALVREKGHRPSHSC, SEQ. I.D. NO. 1, which peptide will raise an antibody response which gives rise to an antibody which is reactive with the p53as but not with p53.